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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/025,335 | 12/18/2001 | Roger Coleman | PF-0198-1 CON | 4775 |

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| EXAMINER | |
|---|---|
| KAUFMAN, CLAIRE M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

DATE MAILED: 05/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/025,335 | COLEMAN ET AL. | |
| | Examiner | Art Unit | |
| | Claire M. Kaufman | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *3-7,9,10,12-16,28 and 29* is/are pending in the application.

4a) Of the above claim(s) *14-16,28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7,9,10,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *3-7,9,10,12-16,28 and 29* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Arguments*

The rejection of claims 3 and 9 under 35 USC 112, second paragraph, for reciting "biologically active" is withdrawn in view of the amendment to the claims.

The rejection of claims 3, 6, 7 and 9 under 35 USC 102(b) as anticipated by Gerard et al. (Nature, 1991) is withdrawn in view of the amendment to the claims.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Response to Amendment*

The Declarations of Drs. Rockett and Iyer under 37 CFR 1.132 filed February 23, 2004, are insufficient to overcome the rejection of claims 3-7, 9, 10, 12 and 13 based upon the rejections under 35 USC 101 and 112, first paragraph, as set forth in the last Office action because: the declarations do not ascertain a specific and substantial or well established utility for the claimed polynucleotide as discussed in the arguments to the rejections below.

### *Claim Rejections - 35 USC § 101*

Claims 3-7, 9,10, 12 and 13 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicants argue (pages 7 and 9) that "The claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease, none of which requires knowledge of how the polypeptide coded for by the polynucleotide actually functions." Stating further that the polynucleotide can be useful without knowledge of its actual biological function or the function of the polypeptide it encodes. The argument has been fully considered, but is not persuasive. "Toxicology testing" is not specifically asserted in the specification; but even if it was, use of the claimed polynucleotide in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual

member of the array. This is a general utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicants' individual polynucleotide(s) was affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. The asserted utility in gene expression monitoring assays is also not substantial, because significant further research would have to be conducted to determine which diseases correlate with altered forms or levels of the claimed polynucleotides and whether the claimed polynucleotides are overexpressed or underexpressed in the diseased tissue. Furthermore, since any expressed polynucleotide can be added to a microarray for gene expression monitoring, the asserted utility is not specific to the claimed polynucleotides. The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a credible, specific and substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696.

The Declaration of Iyer is insufficient to overcome the rejections because while it is not argued that research on patterns of expression using a large number of nucleic acids can provide valuable information, the claimed polynucleotide has no known association to a particular type(s) of cancer/tumor or expression pattern that would negate the need for significant further research by the skilled artisan to determine how the particular claimed polynucleotide expression pattern could be used in accordance with the requirements of 35 USC 101 or 112, first paragraph.

Dr. Iyer states on page 5 of his declaration that, "To provide maximum versatility as a research tool, the microarray should include -- and as a biologist I would want my microarray to include -- each newly identified gene as a probe." The argument has been fully considered, but is not persuasive to overcome the rejection. Just as with using a polynucleotide as a molecular weight marker, the use of a polynucleotide in a microarray is not substantial, providing only a use generally applicable to most polynucleotides. The specification has not linked the claimed polynucleotide with any specific disease state or disorder, as discussed above and in previous Office Actions. Adding the claimed polynucleotide to a microarray would not make the

microarray any more valuable than adding any other "orphan" polynucleotide. The asserted utility is not specific to the claimed polynucleotide.

Dr. Rockett in his declaration discusses (p. 4) the use of polynucleotides in both microarray and non-microarray systems such as subtractive hybridization. The argument has been fully considered, but is not persuasive. It is maintained that until a polynucleotide in, for example, subtractive hybridization is show to be associated with a particular function or disease and how it is so associated (e.g., levels are significantly increased or alternatively spliced form is uniquely associated with it), the polynucleotide has no specific and substantial utility, but is merely a research tool with a use the same as that of a multitude of other polynucleotides. As to the asserted use in a microarray, microarray technology *per se* has patentable utility. However, the microarray is not being claimed, but rather a polynucleotide that can be used in a microarray. The claimed polynucleotide is not disclosed as being expressed at an altered level or form in any diseased tissue as compared to the corresponding healthy tissue. Therefore, the assertion that the claimed polynucleotide has patentable utility as a probe in, or member of, a microarray is not specific. Any orphan polynucleotide can be used in the same way.

***Claim Rejections - 35 USC § 112, First Paragraph***

Claims 3-7, 9,10, 12 and 13 remain also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established, one skilled in the art clearly would not know how to use the claimed invention utility for the reasons set forth in the previous Office action (p. 6).

Applicants state that the arguments directed to the rejection of the claims under 35 USC 101 also pertain to the rejection of the claims under the related rejection under 35 USC 112, first paragraph. As such, the Examiner has addressed them above.

Applicants argue for the rejection of claim 7 as it reads on gene therapy, that the claim is not direct to a method, and the claimed transformed cell may be used for may things besides gene therapy. The argument has been fully considered, but is not persuasive. Even though the cell may be used for methods other than gene therapy, the claim nonetheless reads on a

transformed cell in a human or that is intended to be used for gene therapy in a human. For the reasons set forth in the previous Office action on page 6, it is maintained that it would require undue experimentation to make/use the claimed cell as it reads on use within a human.

Claims 3, 6, 7, 9, 12 and 13 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth on pages 6-7 of the previous Office action.

Applicants argue (page 14) that the specification and the level of skill in the art demonstrate possession of the claimed sequences, citing the USPTO Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, Written Descriptions (1/5/01). The argument has been fully considered, but is not persuasive. The claims do not require that the polynucleotide encode a particular protein with a known or disclosed function or possess any particular functional characteristic, nor possess any particular conserved structure (*e.g.*, conservation of domains with disclosed or recognized function(s)) or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides that is defined only by sequence identity. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Which nucleic acids of the genus comprising the required sequence are part of the invention has not been set forth.

Applicants argue that variants, including "naturally occurring" variants are fully supported in the specification, arguing that, "Given any naturally occurring amino acid or polynucleotide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO:1 or SEQ ID NO:2." The argument has been fully considered, but is not persuasive. The issue is not to recognize if a naturally occurring polynucleotide or polypeptide meets the structural limitations of the claim, but to be able to readily envision which polynucleotides or polypeptides meeting the structural requirements are also naturally occurring given only the knowledge of the structure of SEQ ID NO:1 and 2 and the other diverse naturally occurring prior art polypeptides sharing some structural identity with SEQ ID NO:1 (*e.g.* C5a, 2PY5, FRP). There is insufficient information for the skilled artisan to be able to make this determination without further research. The skilled artisan would not have recognized that the inventors were in possession of the group of claimed naturally occurring polynucleotides and polynucleotides encoding naturally occurring polypeptides.

Applicants argue that the claims specifically define the claimed genus through recitation of chemical structure, citing *Fiers v Revel* and *Lily* for support of the argument that with sufficient structural definition, a function is not necessary for written description. The argument has been fully considered, but is not persuasive. As discussed in the paragraph two above this, while the factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof, the instant application has provided only a partial structure, which is not sufficient in this instance for written description. The only factor present in the claim is a partial structure in the form of a recitation of percent identity. No portion or domain of significance is disclosed, especially no region that must be conserved to maintain a special property of the polynucleotide or encoded polypeptide. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Applicants argue that Brenner et al. (PNAS, 1998) show that 30% sequence identity is enough to establish evolutionary homology between sequences and 40% identity between just 70 amino acids of a protein is enough to signify homology between proteins; and, that based on Brenner's findings, the skilled artisan would expect variants with 90% sequence identity as

currently claimed would have the functional activities of a C5a-like receptor protein. The argument has been fully considered, but is not persuasive. If one knew a function or a ligand of the protein of SEQ ID NO:1 of the instant application, and if the claimed encoding polynucleotides encoded proteins had a disclosed and recited claimed specific function, then such polynucleotides at least 90% identical to SEQ ID NO:2 might be sufficiently described. However, there is no function by which the skilled artisan can judge a functional relationship to the disclosed polynucleotide and encoded nucleic acid. Note that there would remain a written description problem for "naturally occurring" variants.

***Claim Rejections - 35 USC § 112, Second Paragraph***

Claims 3, 9 and dependent claims 6, 7 and 10 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons set forth in the previous Office action on page 8 as they relate to the use of the term "naturally occurring".

Applicants argue that "naturally occurring" in these claims means that the polynucleotide or polypeptide has a sequence found in nature, regardless of the way it was produced. The argument has been fully considered, but is not persuasive. The metes and bounds of the claim cannot be determined because since all naturally occurring sequences meeting the structural limitation are not known or disclosed, one could not discern which polynucleotides or polypeptides recited in the claims have naturally occurring sequences. It is suggested that this rejection could be overcome with an actual product-by-process limitation. For example in claim 3b), '..a polypeptide comprising a sequence 90% identical to ...SEQ ID NO:1, wherein said polypeptide comprising has the same sequence as a polypeptide isolated from nature.'

***Claim Rejections - 35 USC § 102***

Claims 3, 4, 6, 7, 9, 10, 12 and 13 remain rejected under 35 U.S.C. 102(b) as being anticipated by Jacobs et al. (US Patent 5,723,315, #1 cited by Applicants).

Claims 3, 6, 7, 9, 12 and 13 remain rejected under 35 U.S.C. 102(b) as being anticipated by Ruben et al. (WO 98/54206).

The above rejections under 35 USC 102(b) are maintained as set forth in the previous Office action on pages 9-10.

Applicants argue that the instant application is enabled and has utility and receives benefit of the parent filing date of January 31, 1997, so that neither of the above references is applicable as prior art. The argument has been fully considered, but is not persuasive. For the reasons set forth in the previous Office action and as discussed above, it is maintained that the claimed invention does not have utility and neither does the parent application for the same reasons. The effective filing date is the filing date of the instant application (12/18/01).

### *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571)272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 8:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571)272-0871.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Claire M. Kaufman, Ph.D.
Patent Examiner, Art Unit 1646
May 10, 2004

LORRAINE SPECTOR
PRIMARY EXAMINER